

I. AMENDMENTS

IA. AMENDMENTS TO THE SUBSTITUTE SPECIFICATION

Please amend paragraph 0051 of the Substitute Specification, as follows

Chad
B'
~~A compound of the invention is a peptide comprising from 10 to 50 amino acids. The amino~~
acids are preferably one of the twenty naturally occurring L-amino acids. However, D-amino acids may be present as may amino acid analogs. A sequence of the invention will comprise an integrin binding motif such as RGD sequence in either the L- or D- form but preferably in the L-conformation. The peptide of the invention can be amidated or non-amidated on its C-terminus, or carboxylated or non-carboxylated on its N-terminus. The peptide of the invention may or may not contain a glycosaminoglycan binding motif such as SGDG (SEQ ID NO:01) sequence in L- or D-isomer form. A compound of the invention is still further characterized by biological activity i.e. it enhances skeletal growth as well as the growth or recruiting of osteoblast or odontoblast cells on surface of the new skeletal growth.

Please amend paragraph 0052 of the Substitute Specification, as follows:

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B
~~Specific examples of peptides of the invention comprise seven to forty-seven amino acids on~~
either side of the RGD sequence of the naturally occurring sequence of matrix extracellular phosphoglycoprotein. Thus, examples of peptides of the invention comprising sequences taken from the following sequence and including the RGD sequence shown in bold:

DSQAQKSPVKSKSTHRIQHNIDYLNKHLKLVKKIPSDFEKSGYTDLQERGDNDISPFSGDG

~~QPFKDIPGKGEATGPDLEGKDIQTGEAGPSEAESTHL (SEQ ID NO:02)~~

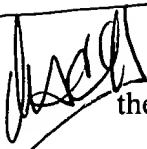
Please amend paragraph 0053 of the Substitute Specification, as follows:

0613 ~~Specific examples of peptides of the invention which comprise the RGD sequence as the~~
terminal sequence include the following:

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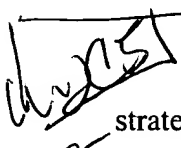
AQKSPVKSKSTHRIQHNIDYLNKHLKSVKKIPSDFEFGSGYTDLQERGD (SEQ ID NO:03)
RGDAQKSPVKSKSTHRIQHNIDYLNKHLKSVKKIPSDFEFGSGYTDLQE (SEQ ID NO:04)
DSQAQKSPVKSKSTHRIQHNIDYLNKHLKSVKKIPSDFEFGSGYTDLRGD (SEQ ID NO:05)
RGDSPVKSKSTHRIQHNIDYLNKHLKSVKKIPSDFEFGSGYTDLQE (SEQ ID NO:06)
DSQAQKSPVKSKSTHRIQHNIDYLNKHLKSVKKIPSDFEFGSGRGD (SEQ ID NO:07)
RGDTHRIQHNIDYLNKHLKSVKKIPSDFEFGSGYTDLQE (SEQ ID NO:08)
DSQAQKSPVKSKSTHRIQHNIDYLNKHLKSVKKIPSDFERGD (SEQ ID NO:09)
RGDLKHLKSVKKIPSDFEFGSGYTDLQE (SEQ ID NO:10)
DSQAQKSPVKSKSTHRIQHNIDYLNKHLKSVKKIPSRGD (SEQ ID NO:11)
RGDLSKSVKKIPSDFEFGSGYTDLQE (SEQ ID NO:12)
DSQAQKSPVKSKSTHRIQHNIDYLNKHLKSRGD (SEQ ID NO:13)
RGDVKKIPSDFEFGSGYTDLQE (SEQ ID NO:14)
DSQAQKSPVKSKSTHRIQHNIDYLNKRGD (SEQ ID NO:15)
RGDIPSDFEFGSGYTDLQE (SEQ ID NO:16)
DSQAQKSPVKSKSTHRIQHNIDRGD (SEQ ID NO:17)
RGDDFEFGSGYTDLQE (SEQ ID NO:18)
DSQAQKSPVKSKSTHRRGD (SEQ ID NO:19)
RGDGSGYTDLQE (SEQ ID NO:20)
DSQAQKSPVKRGD (SEQ ID NO:21)
RGDGYTDLQE (SEQ ID NO:22)
DSQAQKSRGD (SEQ ID NO:23)
~~RGDNDISPFSGDGQPFKDIPGKGEATGPDLEGKDIQTGFA (SEQ ID NO:24)~~

Please amend paragraph 0054 of the Substitute Specification as follows:

 ~~Specific examples of the peptides of the invention which comprise the RGD internally include~~
the following:

B4
NDI RGDSPFSGDGQPFKDIPGKGEATGPDLEGKDIQTGFA (SEQ ID NO:25)
NDISPF RGDSGDGQPFKDIPGKGEATGPDLEGKDI (SEQ ID NO:26)
NDISPFSGD RGDGQPFKDIPGKGEATGPD (SEQ ID NO:27)
FSGDGQPFKDIPGKGEATGPDLEGKDIQTGFAGPSEAES RGDTHL (SEQ ID NO:28)
IPGKGEATGPDLEGKDIQTGFAGPSE RGDAESTHL (SEQ ID NO:29)
EATGPDLEGKDIQTGFAG RGDPSEAESTHL (SEQ ID NO:30)
NDISPFSGDGQPFKD RGDIPGKGEATGPDLEGK (SEQ ID NO:31)
GKGEATGPDLEGKDI RGDQTGFAGPSEAESTHL (SEQ ID NO:32)
FSGDGQPFKDIPGKGEATG RGDPDLEGKDIQTGFAGPSEA (SEQ ID NO:33)
DGQPFKDIPGKGEATG RGDPDLEGKDIQTGF (SEQ ID NO:34)
PFKDIPGKGEATG RGDPDLEGKDIQ (SEQ ID NO:35)
DIPGKGEATG RGDPDLEGKDIQTGFAGP (SEQ ID NO:36)
DGQPFKDIPGKGEATG RGDPDLEGKDIQTGF (SEQ ID NO:37)
GKGEATG RGDPDLEGKDIQTGFAGPSEA (SEQ ID NO:38)
EATG RGDPDLEGKDIQTGF (SEQ ID NO:39)
EATG RGDPDLEGK (SEQ ID NO:40)
~~EATG RGDPDL (SEQ ID NO:41)~~

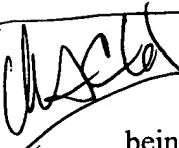
Please amend paragraph 0065 of the Substitute Specification, as follows:

 ~~Six different peptides were manually synthesized by the 9-fluorenylmethoxycarbonyl (Fmoc)~~
strategy and prepared in the C-terminal amide form. The six peptides are as follows:

B5
D-00001: IPSDFEFGSGYTDLQE (SEQ ID NO:42)
D-00002: DFEFGSGYTDLQERGD (SEQ ID NO:43)
D-00003: YTDLQERGDNDISPF (SEQ ID NO:44)
~~D-00004: ERGDNDISPFSGDGQ (SEQ ID NO:45)~~

D-00005: NDISPFSGDGQPFKD (SEQ ID NO:46)
D-00006: TDLQERGDNDISPFSGDGQPFKD (SEQ ID NO:47)
(C-terminus amidated)

Please amend paragraph 0071 of the Substitute Specification as follows:

 ~~The six peptides of Example 1 were tested for their ability to enhance bone growth with the tests~~
being carried out as described above in Example 2. The peptides which did not include the RGD
sequence did not show positive results. The other four peptides showed positive results with the best
results being obtained with the sequences

 D-00004: ERGDNDISPFSGDGQ (SEQ ID NO:45), and

D-00006: ~~TDLQERGDNDISPESGDGQPFKD (SEQ ID NO:47)~~